

# Effect of Pain Induction and Pain Reduction on Conditioned Pain Modulation: a Systematic Review

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## INTRODUCTION and AIM

Pain facilitation and pain inhibition might be present in chronic pain patients. A decreased efficacy of pain inhibition can be measured by conditioned pain modulation (CPM). It is however unclear whether the presence of pain influences the efficacy of endogenous pain inhibition, measured by CPM.

This systematic review aimed to provide an overview of what is known thus far about the influence of clinical (acute and chronic) or experimental pain induction and pain reduction on CPM in adults.

## METHODS

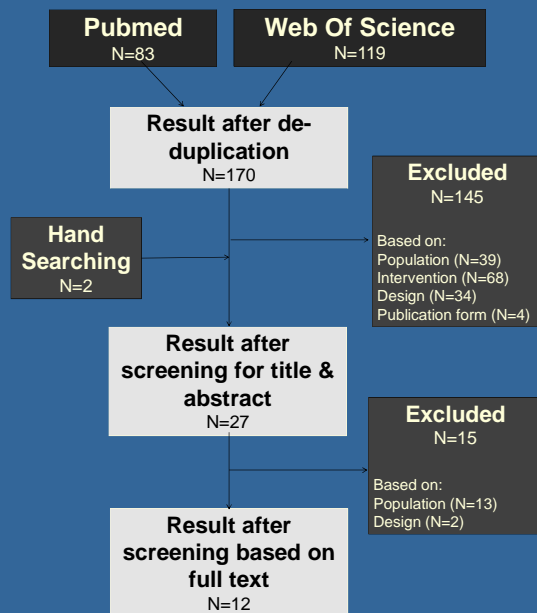


Figure 1. Flowchart of the selection process

### Inclusion criteria:

- discuss the effect of changes in pain on CPM
- RCT's, case control, cohort, cross-over & cross-sectional studies
- adults

The search strategy can be found in figure 1. Checklists of the EBRO platform and a handmade CPM paradigm were used to assess methodological quality.

## RESULTS

**Study characteristics:** mechanical (pressure), thermal (heat or cold), electrical or tactile stimuli were used as test stimulus. The administration sites were very different. A cold pressor test, hot water bath, pressure, CO<sub>2</sub> laser stimulation and Tourniquet test were used as a conditioning stimulus, .

**Methodological quality:** 3 articles got a level 'A2' of evidence, 6 were classified as 'B' and 3 as 'C'.

All studies were divided in 3 groups based on topic: (1) Influence of medication, (2) pain induction in those with (sub)acute pain and experimental pain or (3) the relief of chronic pain (in OA) on CPM efficacy.

### Medication

EFFECT ON CPM	DRUG	STUDY POPULATION
NO	Pregabalin	Chronic Pancreatitis
	Tropisetron	Chronic LBP
NEGATIVE	Dexmedetomidine	Healthy
	Lidocaine & Bupivacaine	Cervical facet pain
	Morphine	Healthy
	Opioids	Chronic pain
	Ketamine	Healthy
	Oral contraceptives	Healthy
POSITIVE	Naloxone	Healthy

### (Sub)Acute and Chronic pain

EFFECT ON CPM	INTERVENTION	STUDY POPULATION
NO	Exercise induced pain	Acute shoulder pain
	Electrical stimulation	Acute Pain in TMJ
POSITIVE	Joint Replacement	Chronic Knee OA
	Joint Replacement	Chronic Hip OA

## DISCUSSION

Different effects of medication on CPM might be caused by **different working mechanisms** of medication. They might work through influence on pain inhibitory pathways or rather work on hyperalgesia.

A lot of chronic pain patients take medication. Lowered CPM responses should therefore be **carefully interpreted**.

In chronic pain reduced CPM response can be restored after removal of the peripheral pain source. Remarkably this was not found in those with acute pain. This might be due to medication use or the fact that **CPM deficiencies** in pain conditions are most likely more related to the **duration** of clinical pain than to pain itself.

Finally, **multiple systems** might possibly be involved in efficacy of CPM and should be taken into account: stimuli administration, gender, cognition, anxiety, follicular phase, comorbidities,...



## CONCLUSION

Some analgesic medications and oral contraceptives might inhibit the CPM mechanism. There is limited evidence that pain relieving surgery improves CPM in chronic pain patients. The results suggest that only in case of already lowered CPM values (like in chronic pain patients), CPM can improve after elimination of pain.

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